

ENZYME-SECRETING FUNCTION OF THE INTESTINE IN DOGS,
AS INFLUENCED BY ADRENALECTOMY AND INJECTION OF SOME
STEROID HORMONES

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For a long time there has been evidence to support a close connection between the condition of the adrenal cortex and the activity of the digestive tract. For instance, the well-known impairment of digestive activity during Addison's disease provides such evidence.

It is widely held that hormones of the adrenal cortex play an important role in the development of general adaptive reactions of the organism to strong nonspecific stimulants. In particular, these hormones can protect the digestive system from the damaging effects of such stimulants. It is also known that hormones of the adrenal cortex can influence a number of important metabolic processes in tissues. In this connection, their influence on the enzyme-secreting function of the intestinal mucosa is of special interest. The mucosa rapidly synthesizes various substances, including highly specific enzymes, and is distinguished under normal conditions by a high rate of regeneration of the epithelium, which is sloughed off into the intestinal lumen during the process of secretion [2, 5, 6].

We attempted to study the enzyme-secreting function of the intestine in dogs, as influenced by adrenalectomy and by making up hormonal deficiencies with parenteral injection of cortisone and deoxycorticosterone (i.e., representatives of the glucocorticoids and mineralocorticoids); and to clarify whether there are any differences in the effects of these two hormones on the intestine under set conditions.

EXPERIMENTAL METHODS

The experiments were carried out on three dogs, in which two isolated loops were formed, one from the duodenum and the other from the lower part of the large intestine (by Thiry's method). After the original level of secretion had been re-established, first one adrenal was removed, and secretion was observed; then, approximately thirty days after the operation, the second adrenal was removed. Afterwards the dogs were given daily intramuscular injections of steroid hormones to maintain vitally important functions: first cortisone and deoxycorticosterone, then cortisone alone, both hormones again, and finally deoxycorticosterone alone. Each period consisted of 15-20 days.

We selected the doses of these hormones in preliminary experiments. By trying out increasing quantities of hormones, we settled on those quantities which produced a good general state of the animals, good utilization of food, normal motility, and absence of visible impairment of digestive activity; in other words, we settled on those quantities of hormones which prevented appearance of clinically expressed symptoms of adrenal insufficiency.

In a period when only one hormone was being injected, the dose of cortisone per kg body weight was 0.41 mg, and the dose of deoxycorticosterone acetate was 0.068 mg. In a period when both hormones were being injected, the dose of cortisone was 0.26 mg, and the dose of deoxycorticosterone was 0.03 mg, per kg.

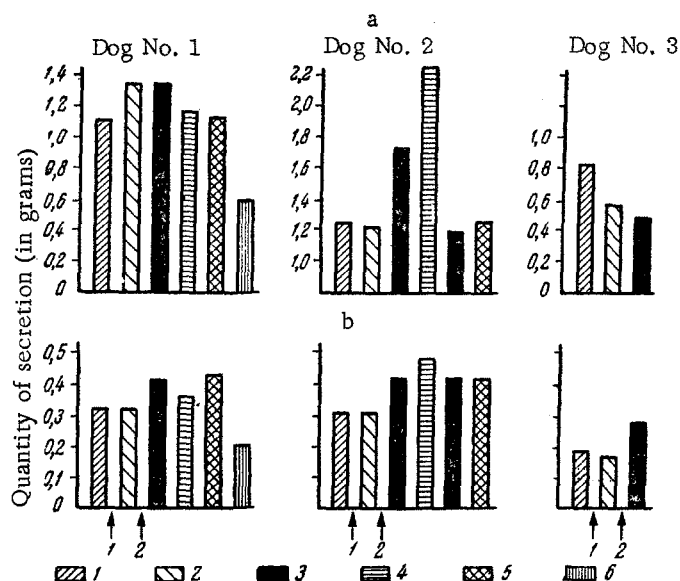


Fig. 1. Quantity of secretion obtained from isolated intestinal loops in one hour. a) Total quantity; b) dense fraction. Arrow 1) Removal of one adrenal, arrow 2) removal of both adrenals. 1) Before adrenalectomy; 2) after removal of one adrenal; 3) after removal of both adrenals and with injection of cortisone and deoxycorticosterone; 4) injection of cortisone; 5) injection of deoxycorticosterone; 6) without hormones.

In external appearance and behavior these dogs did not differ from dogs on which no operations had been performed. Throughout the whole experiment the animals received the usual full amount of food ration. When cortisone alone was being injected, they received in addition 5 g of sodium chloride.

Intestinal secretion in the dogs was studied regularly three times a week. Intestinal juice was collected over the course of five hours during intermittent secretion. The amounts of the fluid and dense fractions were determined quantitatively; then the secretion was homogenized, and the homogenate was analyzed for amounts of the enzymes, enterokinase by the method of G. K. Shlygin [4], alkaline phosphatase by splitting of sodium phenolphthalein phosphate [3], saccharase by splitting of cane-sugar (using a polarimetric method), and peptidase by splitting of peptone, followed by titration of carboxyl groups with 0.2 N potassium hydroxide in a 90% alcohol solution (for further details see [1]).

EXPERIMENTAL RESULTS

After removal of one adrenal (without supplementary injection of hormones) the quantity of secretion (in particular, its dense fraction) obtained from isolated loops of the intestine in dogs underwent no significant change.

However, the quantity of some enzymes (computed per unit weight of the secretion) fell noticeably. This was particularly true of enterokinase and saccharase, whose concentrations decreased in some dogs by 40-50%. On the other hand, the content of peptidase (total determination) showed a tendency to increase in some dogs (Figs. 1 and 2).

After removal of the second adrenal, followed by regular injection of cortisone and deoxycorticosterone, changes were observed both in enzyme secretion and in the quantity of intestinal juice (see Fig. 1). The total

quantity of juice generally increased. Thus, for instance, the quantity of juice from dog 1 rose on the average from 1.12 to 1.37 g per hour. One's attention is particularly caught by the increased secretion of the "dense" fraction of intestinal juice, consisting primarily of epithelial cells sloughed off by the mucosa. The secretion of this fraction of intestinal juice rose significantly (for instance, in dog 1, from 0.32 to 0.42 and sometimes to 0.62 g per hour). In Fig. 1 these changes are illustrated by average values, computed from 5-10 determinations in each experimental period.

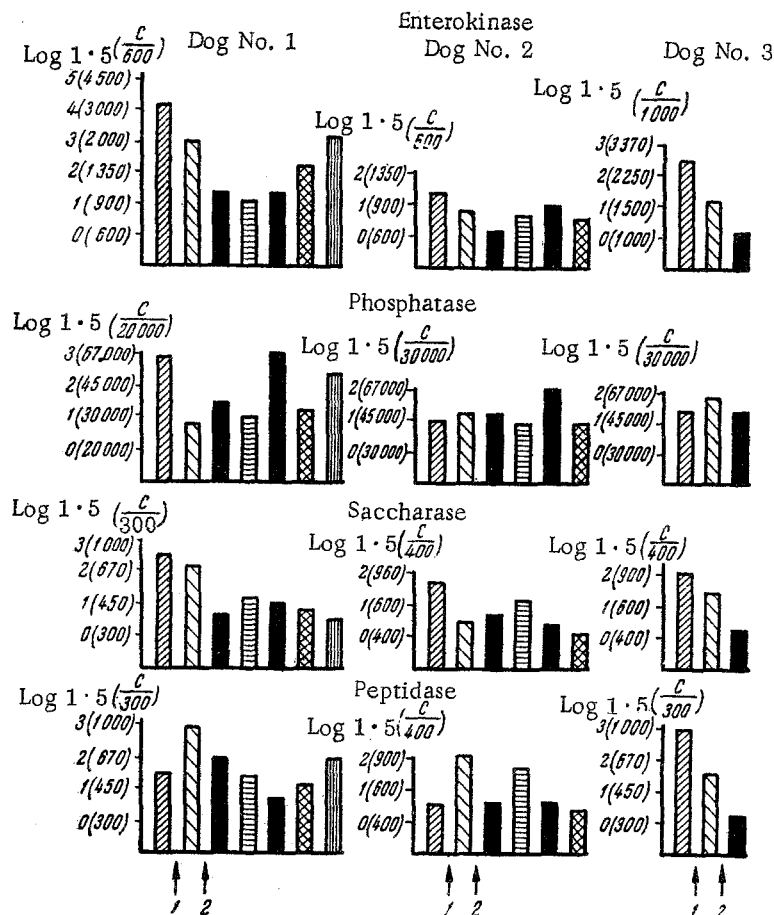


Fig. 2. Content of enzymes (in relative units) in 1 g of the "dense" fraction of intestinal secretion. Symbols same as in Fig. 1. c) content of enzyme.

We also determined the amount of nucleic acid in the collected secretion (by the method of Schmidt and Tannhauser). Nucleic acid content per unit weight of the "dense" fraction of juice did not change significantly, and this indicates that the relative content of cellular elements in this fraction did not change. Hence, it is probably that the increased amount of the "dense" fraction is connected with more rapid sloughing off of the intestinal epithelium.

Changes in enzyme content of the secretion after removal of the second adrenal followed the same pattern as after removal of one adrenal, but changes were more sharply expressed. The content of enterokinase (per g of secretion) declined by a factor of more than 2, in comparison with the original level (Figs. 2 and 3). The saccharase content also decreased sharply, while the concentration of alkaline phosphatase frequently remained unchanged and declined in only one dog. The content of peptidases was close to the level in the original period. Despite the increased secretion of the "dense" fraction of juice, the quantity of enterokinase and saccharase secreted per hour underwent a significant decrease (Fig. 3).

These changes in secretion of juice and enzymes were basically confirmed and extended when cortisone alone or deoxycorticosterone alone was injected, instead of both hormones. Some slight differences were that

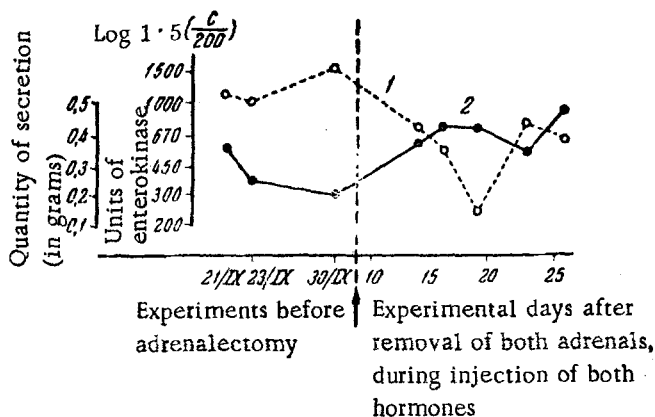


Fig. 3. Changes in the quantity of the "dense" fraction of the secretion and the content of enterokinase in this fraction (in units per g) after adrenalectomy, during injection of cortisone and deoxycorticosterone. Dog No. 2. 1) Enterokinase content in the "dense" fraction of the secretion; 2) quantity of the "dense" fraction of the secretion; both adrenals were removed at the arrow. c) content of enterokinase.

was killed five days after injection of hormones had ceased. Dog No. 3 died as a result of sudden appearance of symptoms of cardiac motor failure, a month after removal of both adrenals, during which period she received both hormones. At post-mortem it was noticed that the mucosa of the stomach, small intestine, and large intestine of this dog was saturated with blood. There were no visible changes in other organs. In all dogs a lowered level of enzymes in scrapings from the mucosa of various parts of the intestine was noticed.

Quantity of Juice (in g per hr) and of Enzymes (in Relative Units) After Injection of Hormones had Ceased (Dog No. 1)

Day after injection of hormones had ceased	Juice secreted per hour		Enzymes secreted per hour			
	total quantity	"dense" fraction	enterokinase	phosphatase	saccharase	peptidase
3rd	0.82	0.29	820	12456	113	186
4th	0.74	0.23	614	16906	102	156
5th	0.25	0.10	105	3797	31	—

Thus, removal of one or both adrenals leads to similar changes in the enzyme-secreting activity of the intestine, the chief differences being in the extent of their appearance. In the first case, of course, reduced adrenal function sets in; however, when both adrenals are removed and cortisone plus deoxycorticosterone are injected (together or separately), a certain degree of adrenal insufficiency evidently still arises.

First of all, injection of these two hormones might not be equivalent to their normal secretion, but more important, while these hormones can maintain the general clinical condition of the animals, they cannot replace the whole complex of hormones produced by the adrenal cortex and, therefore, they cannot maintain all functions which are in one way or another influenced by this hormonal complex.

saccharase content in the secretion gradually increased during injection of cortisone alone, and decreased again during injection of both hormones (see Fig. 4). The content of alkaline phosphatase was somewhat higher in the period of application of both hormones than in periods of injection of either hormone alone (see Fig. 2).

At the end of experiments on one dog (No. 1), injection of hormones was stopped. At this point the total quantity of juice and, in particular, the quantity of the "dense" fraction increased, especially at the end of the five-day period of observation (see the table). At the same time, the concentration of enterokinase in the secretion declined significantly.

In all dogs blood also appeared in the "dense" fraction of the secretion after removal of both adrenals. In one of the dogs this was distinctly observable, even after removal of one adrenal.

At the end of this series of experiments, when dog No. 2 had been sacrificed and was being dissected, a certain degree of hemorrhage into the mucosa of the small intestine was noticed. This same finding was more apparent in dog No. 1, which

As we have seen, this level of adrenal insufficiency chiefly decreases the output of the most specific extracellular enzymes of the intestine, enterokinase, and saccharase. The least effect is upon secretion of intracellular enzymes, such as peptidase, whose content in the secretion even shows a tendency to increase.

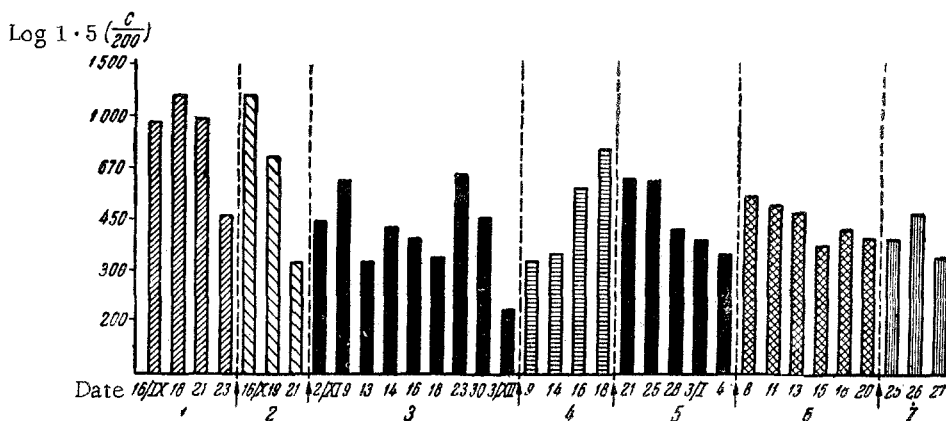


Fig. 4. Saccharase content in the dense fraction of the secretion. Dog No. 1. 1) Before adrenalectomy; 2) after removal of one adrenal; 3) after removal of both adrenals, during injection of the two hormones; 4) injection of cortisone; 5) injection of the two hormones; 6) injection of deoxycorticosterone; 7) without hormone. c) content of saccharase.

We also observed changes in other aspects of secretory activity of the intestinal mucosa, expressed as increased secretion of the "dense" fraction of intestinal juice (basically, epithelial cells sloughed off in the process of secretion) and regular appearance of blood in the "dense" fraction of juice.

These results permit one to conclude that the adrenal cortex plays an important role in regulating a number of aspects of the enzyme-secreting function of the intestine, by its output of hormones; the adrenal cortex stimulates formation and secretion of the most specific intestinal enzymes at a high level, checks secretion of the "dense" (cellular) fraction of juice, and also maintains the integrity of the blood vessels in the intestinal mucosa.

Further experiments are necessary to clarify the mechanism of this effect of the adrenal cortex.

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SUMMARY

As established in experiments on dogs with isolated intestinal sections, the amount of the "solid" portion and the total secretion per time unit exhibited no significant changes after unilateral adrenalectomy; however, the enterokinase and saccharase content in the secretion showed a marked drop. After bilateral adrenalectomy and administration of cortisone and desoxycorticosterone the amount of secreted "solid" portion of the intestinal juice becomes greater, whereas the enterokinase and saccharase content is considerably diminished. There is a tendency towards the peptidase content increase. The main features of these changes are retained if cortisone or desoxycorticosterone alone is administered for a period of 10 days, although in such conditions there occur some variations in the secretion of individual hormones. Without hormone administration the total amount of intestinal secretion and of its "solid" portion, as well as the quantity of enzymes secreted per time unit gradually decreases. After bilateral adrenalectomy blood is always present in the "solid" portion of the secretion.

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All abbreviations of periodicals in the above bibliography are letter-by-letter transliterations of the abbreviations as given in the original Russian journal. *Some or all of this periodical literature may well be available in English translation.* A complete list of the cover-to-cover English translations appears at the back of this issue.
